significance of the treatment effect was dramatic, increasing the perceived benefit in EPIC and decreasing the benefit in IMPACT-II, GUSTO-IIb, and PURSUIT.

Conclusion: A central adjudication process can have a substantial impact on the overall event rates and trial results. Differences in event rates may reflect systematic differences in identification of suspected events, application of criteria used for events such as reinfarction, or understanding of the most clinically relevant measure. These findings have important implications for future trials.

9:00

837-3 Sustained Platelet GP IIb/IIIa Blockade With Oral Orbofiban: Interim Pharmacodynamic Results of the SOAR Study

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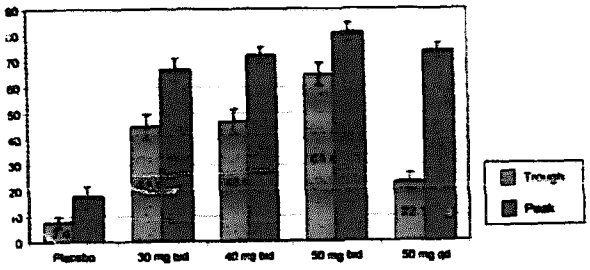
Background: SOAR (Safety of Orbofiban in Acute Coronary Research) is a randomized, placebo-controlled study conducted to compare four dosage levels of the oral platelet GP IIb/IIIa inhibitor Orbofiban to placebo in patients with unstable angina or recent (>6 hours but ≤120 hours) myocardial infarction. Patients (n = 259) were randomized to receive Orbofiban (30, 40, 50 mg BID or 50 mg QD) or placebo for up to 3 months. All patients received concomitant aspirin (162 mg/day).

Methods: Ex vivo inhibition of platelet aggregation to agonist (20 μM ADP) was measured on Day 1 and at 2 and 4 weeks (n = 145).

Results: The inhibition of platelet aggregation to ADP at trough and peak following 2 weeks of dosing were similar to the 4 week results shown below:



Conclusion: Orbofiban produced a dose-related increase in ADP 20μM platelet aggregation inhibition. Target therapeutic ranges of platelet inhibition (60–80% and 40–60% throughout the dosing interval) are achievable with BID dosing.

9:15

837-4 Clinical Efficacy of Integrilin in Unstable Angina is Accompanied by a Modest Increase in Hemorrhagic Risk: The PURSUIT Trial

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Background: Integrilin™ (Eptifibatide), a cyclic KGD peptide inhibitor of the platelet GP IIb/IIIa receptor, was evaluated in the randomized, double-blind, placebo-controlled PURSUIT trial among 10,948 pts with unstable angina. Eptifibatide treatment (180 μg/kg bolus, 2.0 μg/kg/min infusion) for up to 72–96 hrs was associated with an absolute 1.5% reduction in the incidence of death or MI within 30 days (15.7 vs 14.2%, p = 0.0424).

Methods: Bleeding complications during the hospitalization period were defined as severe (intracranial or causing hemodynamic compromise), moderate (requiring transfusion), or mild (all other).

Results/Conclusions: Moderate or severe bleeding (most often at sites of vascular access) was increased with eptifibatide, particularly in pts who did not require bypass surgery. Thus, reduction in ischemic events with eptifibatide is achieved at the cost of a modest increase in clinically-significant bleeding and transfusions, but no increase in intracranial hemorrhage.

	Placebo	Eptifibatide
Moderate or Severe Bleed	9.9%	12.8%*
Moderate or Severe Bleed w/o CABG	2.0%	5.2%*
RBC or Whole Blood Transfusion	9.3%	11.8%
Transfusion w/o CABG	1.8%	4.4%
Intracranial Bleed	0.09%	0.11%

*p < 0.0001

9:30

837-5 Thrombocytopenia With GP IIb/IIIa Inhibitors: A Meta-Analysis

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Background: Thrombocytopenia (↓Plt) is an important complication of glycoprotein (GP) IIb/IIIa inhibitors. Summary data comparing rates to placebo and between agents is sparse.

Methods: We performed a meta-analysis of all placebo-controlled phase II–III clinical trials of GP IIb/IIIa inhibitors using the DerSimonian and Laird random effects model to estimate the odds ratio of ↓Plt for drug vs placebo. Subgroup analyses stratified by drug and required use of heparin were also performed.

Results: Data on ↓Plt was available for 25 of the 26 trials identified. Absolute rates of ↓Plt ranged from 0%–12% depending on the clinical scenario and drug. The overall pooled rate of ↓Plt for 13,093 patients treated with GP IIb/IIIa inhibitors was 2.3%. Odds ratios with 95% CIs for risk of ↓Plt are shown below for selected drugs, trials with vs. without required heparin, and the overall meta-analysis.

Conclusions: Use of GP IIb/IIIa inhibitors increases the risk of ↓Plt by approximately 42% compared to placebo. Current studies do not demonstrate significant differences between drugs, or in the presence or absence of heparin. Heparin, in combination with a GP IIb/IIIa inhibitor, increases the observed absolute rate of ↓Plt, but does not synergistically increase the risk.

	# pts*	OR	95%CI
Abciximab	6,342	1.76	(0.92, 3.37)
Tirofiban	7,158	1.63	(0.94, 2.81)
Eptifibatide	4,618	1.04	(0.60, 1.80)
Lamifiban	3,000	0.83	(0.20, 3.49)
heparin required	12,781	1.38	(0.88, 2.16)
heparin not required	8,799	1.46	(0.92, 2.32)
All trials	*21,580*	*1.42*	*(1.07, 1.89)*

*includes all placebo and treated pts

9:45

837-6 Value of Troponins in Predicting Therapeutic Efficacy of Abciximab in Patients With Unstable Angina

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Background: In patients (pts) with acute coronary syndromes microembolization from ruptured atherosclerotic plaques may cause minor myocardial injury detectable by circulating troponins. This was shown to be associated with an adverse short and long term outcome. The CAPTURE trial demonstrated that platelet inhibition with abciximab reduces risk for myocardial infarction (AMI) and death in pts with refractory unstable angina prior to and after PTCA. The present study therefore investigated whether troponin T (cTnT) allows to predict this benefit.

Methods and Results: In 226 of 546 (41%) pts receiving abciximab and 219 of 547 (40%) pts receiving placebo cTnT ≥0.10 ng/ml) was found on study entry. Event rates (death, AMI) during the 24 to 36 hours treatment phase before coronary interventions:

	cTnT neg	CTnT pos	p-value
abciximab	0.6%	0.9%	ns
Placebo	0.9%	4.1%	p = 0.03
p-value	*ns*	*p = 0.03*	

During the following PTCA abciximab reduced risk in cTnT pos. as well as cTnT neg. pts (4.8% placebo vs. 1.9%, p = 0.04)

Conclusions: cTnT identifies pts with unstable angina who benefit from abciximab through eliminating excessive risk prior to PTCA. Therefore, it may serve as a marker to initiate this treatment. All pts benefit equally from abciximab during interventions.